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Multicenter Nit-Occlud® PDA-R Patent. Ductus Arteriosus Occlusion Device Trial: Initial and Six-Month Results

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Background: Transcatheter closure of a moderate to large patent ductus arteriosus (PDA) using conventional techniques is challenging. The Nit-Occlud® PDA-R trial can close a PDA up to 8 mm in diameter. We sought to report procedural and six-month efficacy and safety results of the multicenter Nit-Occlud® PDA-R trial. Methods: From June 2010 to February 2011, 43 patients were enrolled in three centers from Argentina. Median age was 4.5 (range 1.4–18.4 years) years old at catheterization, 70% were females and weight was 17.7 (range 10–67 kg). Results: PDAs mean diameter was 2.98 ± 1.03 and ranged from 2 to 6.19 mm. About 11.6% were large (≥4 mm), whereas 32.6% were <2.5 mm. Median pulmonary artery mean pressure was 17 mm Hg (range 9–26 mm Hg). The device was implanted successfully in all patients. By echocardiography, trivial residual shunt was observed in 42% at the end of the procedure, in 28% at 24 hr, in 12.1% at one week, and none at three-months. There was one case of embolization (due to undersizing), that was treated successfully with a larger study device. There were no major short- or long-term complications. Conclusions: PDAs ranging from 2 to 6 mm can be effectively and safely closed using the Nit-Occlud® PDA-R device, with good procedural and six-month results. The Nit-Occlud® PDA-R emerges as an optimal alternative for closure of small to moderate PDAs. © 2015 Wiley Periodicals, Inc.

Key words: patent ductus arteriosus; percutaneus closure; PDA-R occluder

INTRODUCTION

With the advent of transcatheter occlusion of patent ductus arteriosus (PDA) more than two decades ago [1–3], new occluding devices continue to arise in an attempt to improve on the limitations of current systems. Early generations of PDA closure devices required very large delivery systems and highly skilled operators for accurate placement and avoidance of hemodynamic instability [4,5]. Potentially desirable improvements may reduce vascular injury, improve the ease and accuracy of positioning and deployment, or improve ductal closure. The ability to remove a partially or fully deployed occluding device may be of particular interest when the initial implant positioning is suboptimal. We describe a multicenter pilot experience with the Nit-Occlud® PDA-R (pfmmedical, Köln, Germany), a novel PDA occluding device.

METHODS

A prospective, multicenter, observational study was conducted in three pediatric tertiary care centers from Argentina. Three operators (MG, LT, and AP), one from each center, had performed all invasive procedures. The protocol (COL-PFM-PDA-07/09) was approved by the Institutional Review Boards of the participating hospital centers. From June 2010 to February 2011, 43 patients underwent anterograde transcatheter PDA closure with Nit-Occlud® PDA-R. Patients were included if they had an echocardiography

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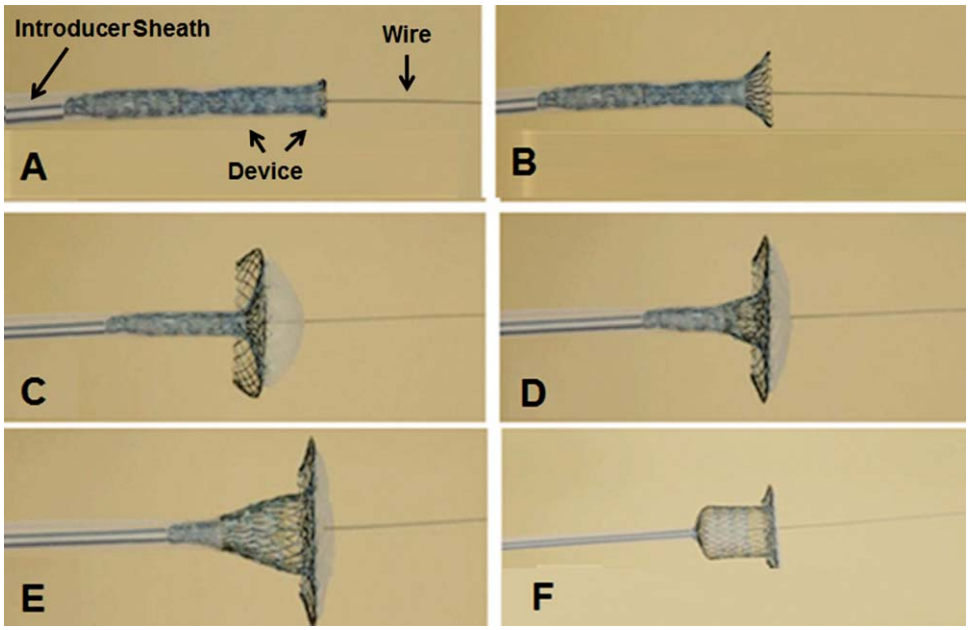

Fig. 1. Ex vivo demonstration of deployment and loading of the device. A–F: Note the rolling motion of Nit-Occlud® PDA-R. Loading of the device works in reversed order. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

diagnosis of PDA (minimal diameter ranging from 2 to 8 mm), left atrium and left ventricle enlargement by echocardiography, and a continuous murmur at physical examination. Exclusion criteria included: (a) weight less than 6.0 kg, (b) pulmonary vascular resistance greater than 8 Woods units, (c) recent serious infection, (d) associated cardiac anomalies that would require cardiac surgery, (e) unable to tolerate sedation, and (f) patients with significant hematologic or oncologic conditions.

Device

Details of this device have already been described [6,7]. Briefly, the Nit-Occlud® PDA-R consists of a one-piece 0.006 inch nitinol wire mesh with very low radial force (9 N, 30% lower than the Amplatzer Duct Occluder), making it less traumatic and superelastic. To ensure PDA occlusion, the implant is manufactured with some synthetic membranes (polyester) fixed with a thread of polypropylene (commonly used in cardiac surgery). The device consists of one retention disc and a stent (Fig. 1A–F). The retention disc has a reversed configuration, as it is designed for anchoring at the aortic ampulla. The device has a very flexible delivery system that consists of an outer wire that makes a loop around a very thin movable central wire. The central wire is connected to the device itself. This delivery system makes the device fully retrievable and repositionable prior to its release. The device is sized according to the external stent diameter, which has to be 1.5–2 times larger than the minimum diameter of the defect. Several device sizes enable occlusion of PDAs from 2 to 8 mm in diameter (Table I) [6].

Procedure

All examinations were performed under general anesthesia or deep sedation, according to operator's discretion. Heparin at the dose of 100 IU/kg and antibiotic prophylaxis were administered. Vascular access was obtained inserting a 4-F sheath into the femoral artery and vein. Aortography was performed using a 4-F NIH or pigtail catheter to document the PDA. Pressure gradients proximal and distal to the PDA were measured in both the pulmonary artery and the aorta before and after device placement. Angiographic measurements of the dimensions of the PDA were collected. The angiographic type of PDA was defined in accordance with the classification by Krichenko et al. [8].

The implantation procedure was performed under fluoroscopy. Through the venous sheath, a 4-F delivery catheter was passed through the PDA to position a guidewire in the descending aorta. Then a delivery sheath (range 5–7 F) was exchanged over the wire from the venous side. The device was threaded onto the delivery cable, immersed in saline, and withdrawn into the loader. The loader was then connected to the delivery sheath and the device was gently advanced through the delivery sheath until the disk is visualized

TABLE I. Device Availability With Measures of the Parts and Recommended Introducer

Device number/indicated for PDA-(MD)	Retention disc (mm)	Stent (mm)	Length (mm)	Number of membranes	Introducer size (F)
2	8	4	6.5	2	5
3	10	5.5	7	2	5
4	12	7	9	3	5–6
5	14	8.5	10	3	6
6	16	10	11	4	7
7	18	11.5	12	4	7
8	20	13	13.5	4	9

Fr, French; MD, minimum diameter; PDA, patent ductus arteriosus.

in the aorta. After the waist of the system was partly configured, the system was pulled back into the PDA (Fig. 2A–D).

While fixing the retention disc in optimal position, the long sheath was then pulled back to deliver the remainder of the device. At this stage, the device was entirely configured and its position was verified by using a contrast injection through a catheter in the aorta as was shown in Fig. 2B. If the device position was ideal, the security seal was cut and the device released by pulling back the central wire. At any point prior to complete withdrawal of the central wire, the device can be pulled back into the delivery sheath and redeployed. The central wire helps to maintain position across the PDA when this maneuver is performed. A final angiogram was performed 15 min after release of the device (Fig. 2D). A chest X-ray and echocardiogram were performed prior to discharge. Follow-up examinations included a clinical and echocardiographic examination at 7 days, one month, 3 months, and 6 months after the implantation.

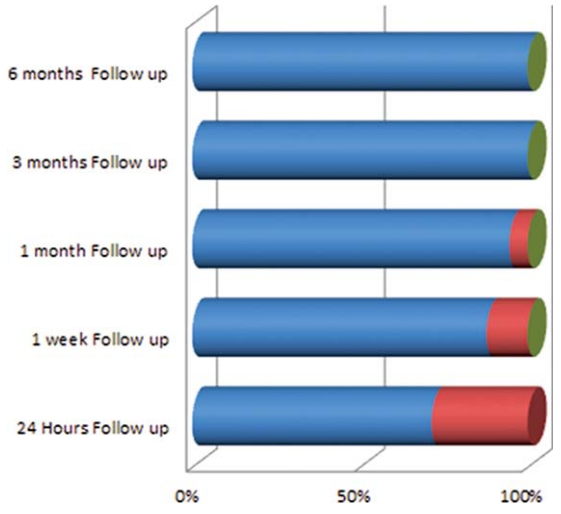

Fig. 2. Closure of a moderate-size PDA. A: The PDA in the lateral view. Note the retention disc located at the ductal ampulla in close proximity to the minimal ductal diameter. The two platinum makers at two edges of the ductal ampulla can be easily detected and improve visibility. B: The stent is unfold inside the ductus. The device is not yet released and remains connected to the delivery wire. C: Angiography after complete configuration of the NitOcclud PDA-R. D: Contrast angiogram performed 15 min after device deployment demonstrating no residual shunt. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Statistical Analysis

Continuous variables are described as mean ± SD or medians with interquartile range. Categorical variables are described by frequencies and percentages. Statistical analyses were performed using the SPSS 20.0 (SPSS Inc., Chicago, IL).

RESULTS

Baseline demographic and angiographic characteristics are listed in Table II. Median age was 4.5 (range 1.4–18.4 years) years old at catheterization, 70% were females and weight was 17.7 (range 10–67 kg, Table II). PDAs mean diameter was 2.98 ± 1.03 and ranged from 2 to 6.19 mm. About 11.6% were moderate or large (≥4 mm), whereas 32.6% were <2.5 mm. The most common device used was no. 5 (retention disc 14 mm, stent 8.5 mm, and length 10 mm) implanted in 10 patients. Transcatheter closure was achieved in all cases. Device was successfully deployed in all but one case, in which the device embolized due to undersizing. Initially, a no. 2 device (retention disc 8 mm, stent 4 mm, and length 6.5 mm) was used but the duct was much larger (5 mm). The device embolized to the descending aorta and it was captured by a 10-mm

TABLE II. Clinical Characteristics and Angiographic Data

	Population, $N = 43$
Age, years	4.5 (1.4–18.4)
Females (%)	70
Weight (kg)	17.7 (10–67)
Height (cm)	111 ± 25
Type of PDA (%)	
A	36 (83.8)
B	(5)11.6
C	2.3
D	0
E	2.3
PDA length (mm)	8.6 ± 2.8
PDA diameter (mm)	2.98 ± 1.03
PDA diameter at the aortic side (mm)	9.6 ± 3.4
Baseline systolic/diastolic aortic pressure (mm Hg)	81 ± 10/43 ± 8
Baseline systolic/diastolic pulmonary pressure (mm Hg)	27 ± 5/13 ± 4

Variables are expressed as mean ± standard deviation or as median (range) or as *N* (%).

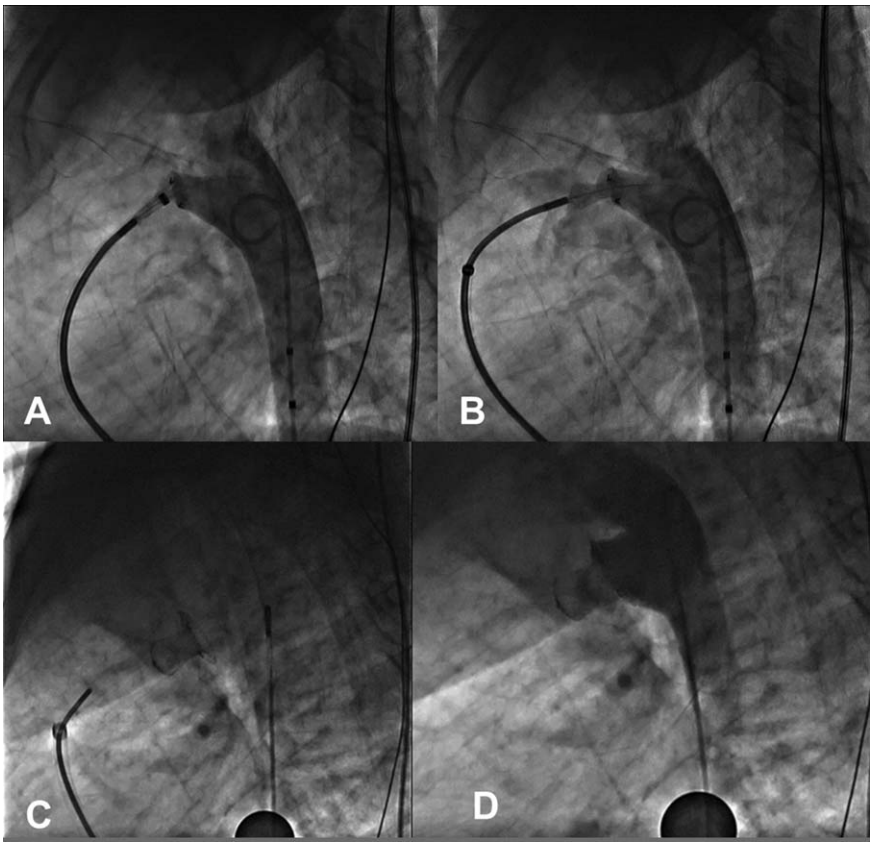

Fig. 3. Rates of complete ductal closure according to time of follow-up.

Amplatz GooseNeck® Snare (ev3 Inc., Plymouth, MN) and retrieved through a larger (6 F) introducer sheath at the right femoral vein. Retrieval was easy due to flexibility and softness of the device. In the same procedure, a no. 4 study device (retention disc 12 mm, stent 7 mm, and length 9 mm) was placed through the 6 F sheath with success and no major adverse events. Immediate closure or minimal residual shunting was achieved in 98% of the patients at 15 min angiography. By echocardiography, trivial residual shunt was observed in 42% at the end of the procedure, in 28% at 24 hr, in 12.1% at one week, and none at three-months (Fig. 3). In one case, a large residual shunt was observed after deployment but it was found to be trivial at 24 hr. There were no signs of postprocedural left pulmonary artery obstruction either by angiography or echocardiography. Furthermore, aortic encroaching was not observed.

DISCUSSION

Currently, catheter closure constitutes the dominant strategy for the treatment of PDA >2 mm and ≤ 8mm in size [5,9]. Several devices and coils have been developed for PDA closure. Initially, the major drawbacks of previous devices and coils were their high incidence of residual shunt, the complexity of the delivery systems, and inability to close larger PDAs [3,4,10]. Newer generations have improved their efficacy but repositioning was still cumbersome. A novel device for percutaneous closure of a PDA should have a user-friendly delivery system with simple mechanics, remain stable during and after deployment, and obtain a high complete closure rate. Similarly, it should require small introducer sheath. The study device comes preassembled by the manufacturer, possess a user-friendly "wire-pulled out" delivery system that permits recapturing and repositioning prior to final release. A single safety wire crosses the device through wire loops that rap around the device. After obtaining a satisfactory position of the device, pulling this wire smoothly releases the device. Providing the wire crosses the stent loops, the device can still be recovered with the long sheath. This feature enhances the safety of the device. Furthermore, accidental detachment of the device from the delivery system requires a large amount of force ($\geq$ 100 N); hence, it is very unlikely to occur. In contrast to the Amplatzer Duct

Occluder I (ADO I, AGA Medical, Golden Valley, MN), proper release of the device requires only a small amount of force (5N) without significant longitudinal traction and allows for an accurate visualization of the device position prior to final release. The ADO I, on the other hand, is released by unscrewing the delivery cable, which can lead to premature release [11].

Due to its enhanced flexibility and spongy-like nature, snaring the study device (in the event of embolization) appears simple and possibly safer than with the ADO I. Anchoring to the aortic ampulla is very efficient and safe with the study device due to the reverse configuration of the retention disc (Fig. 1). Similar to the ADO I (AGA Medical, Golden Valley, MN), the Nit-Occlud® PDA-R is only introduced in an anterograde fashion and achieves complete closure by generating a physical obstruction (stenting of the ductus) and thrombus formation. However, ADO I has higher immediate duct closure rates and can be used to close large PDAs (up to 16 mm). To guarantee complete occlusion of the heart defect, the study device has been built with several synthetic membranes (polyester, Table I) fixed with a thread of polypropylene. In our study, closure rate with the studied device was very high. As demonstrated in this multicenter trial, the device is extremely efficacious at closing not only smaller (<2.5 mm) PDAs but also moderate (2.5–6 mm) ones. At six-month follow-up among patients who have been evaluated, there has been 100% occlusion documented. These findings are most encouraging when reviewing both the size and shapes of the PDA closed in the present report. As noted earlier, the median ductal diameter was 2.98 ± 1 mm, and 11.6% were over 4 mm in diameter. Additionally, nearly every single shape of ductus that has been previously described was seen and closed in this trial using the Nit-Occlud® PDA-R. Nonetheless, in the present study, there was only one case of a tubular PDA. Probably, this type of ducts may be best served with an Amplatzer™ Vascular Plug. In keeping with our findings, a recent PDA study [6] reported a series of 51 high-altitude patients with large PDAs (mean size 4.6 mm, 25% being larger than 6 mm) who underwent successful catheter closure with Nit-Occlud® PDA-R, demonstrating complete shunt closure rates in all patients at one-year follow-up despite high baseline systolic pulmonary artery pressure.

The present system requires small introducer sheaths for the smaller-diameter devices (sheath size 5–7 F for PDA <8 mm in size), which makes this device appropriate for use in small children. It should also be noted that the majority of PDAs in our trial were closed using only a 6 F venous sheath. As a result, there were no vascular complications. Importantly, the ADO II (AGA Medical, Golden Valley, MN) allows catheter closure of small to moderate PDAs with even smaller sheaths (4–5 F) and enables device deployment in a retrograde fashion. Device embolization was observed in one patient without major adverse events. Had the size of the device been appreciated more clearly, device embolization in one patient would have likely been prevented in the present study.

Limitations

This is a small, however, multicenter observational study, which did not aim to demonstrate any superiority in outcomes compared with other closing devices for patients with PDA. However, it represents the largest series of consecutive low-land patients with PDA (2–6 mm), without selection, undergoing the procedure with Nit-Occlud® PDA-R.

CONCLUSION

In the present study, PDA closure with the Nit-Occlud® PDA-R was safe and effective in most patients with PDA up to a diameter of 6 mm, showing a low incidence of residual shunt. The Nit-Occlud® PDA-R might be a good alternative for closure of small to moderate PDAs.

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